Clinical Treatment for Opioid Dependence: Methadone

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Opioid Dependence

- Chronic, often relapsing, biopyschosocial brain disorder
- Contributes to major medical problems, including HIV, hepatitis, tuberculosis
- Between 500,000 and 1 million Americans are believed to be opioid dependent at any point in time
- More prevalent in men by a ratio of 4:1

Opioid Dependence

- Frequent coexisting mental health disorders, especially depression and anxiety
- Often linked to a history of drug-related criminal activity
- Antisocial personality disorder more prevalent in opioid dependent individuals

Treatment Options for Opioid Dependence

- Methadone is the most widely known pharmacologic treatment for opioid dependence
- Cost effective in reducing illicit opioid use, retaining patient in treatment, and reducing illegal drug use
- Reduces the risk of HIV, hepatitis B (HBV), and hepatitis C (HCV)

Treatment Options for Opioid Dependence

- Buprenorphine (Suboxone, Subutex), partial agonist
- Levo-alpha-acetylmethadol (LAAM), no longer available in the United States due to cardiac rhythm problems
- Naltrexone (Trexan), opioid antagonist, poor compliance and retention rates
- Rapid detox (Waismann method)

Federal Regulatory Requirements for Methadone Therapy

- Minimum age 18 years old
- Exception for patients 16 to 18 years old with a documented history of two prior unsuccessful treatment efforts, such as detox or rehab, and parental consent
- At least one year of physiologic dependence (exception for pregnancy)
- Meet criteria for opioid dependence

DSM IV-TR Criteria
Opioid Dependence

At least three of the following criteria must occur within a 12 month period:

1. Tolerance
2. Withdrawal
3. Opioid use in greater quantities or for longer periods of time than intended
4. Unsuccessful attempts to quit or cut down on opioid use

DSM IV-TR Criteria
Opioid Dependence

5. Considerable time devoted to acquiring opioid drugs, using opioid drugs, or recovering from opioid drugs (sometimes referred to as loss of control)

6. Interference with social, occupational, or recreational activities

7. Continued use despite consequences of opioid drugs

Methadone Therapy

- Traditionally provided through methadone maintenance programs, which provide dosing, counseling services, and drug testing
- Currently available in 42 states, the District of Columbia, Puerto Rico, and the Virgin Islands
- Cost of treatment around $4000 annually and sometimes subsidized by insurance or Medicaid
- Also available through general medical practice, but must meet same requirements for MMT

Office-Based Opioid Therapy (OBOT)

- Less restrictive alternative to providing methadone therapy
- Established by federal regulations in 1999
- Primary care physicians able to provide methadone therapy within comprehensive medical practice
- May incorporate up to 30 patients into the practice

Office-Based Opioid Therapy (OBOT)

- Must have training in addiction medicine
- Must be affiliated with a methadone clinic or be monitored by the medical director of a methadone clinic
- Eligible patients are referred exclusively from methadone clinics and must have three years of successful MMT
- Can dispense up to a 30 day supply of methadone

Principles of Medical Management

Achieve Adequate Steady-State Dosing

- Begin induction phase
- Establish maintenance dose
- Avoid medications that affect metabolism of methadone
- Evaluate need for continued maintenance or detox

Principles of Medical Management

Prevent Relapse

- Educate patient and family about relapse
- Encourage involvement in Narcotics Anonymous and Nar-Anon
- Monitor patients for intoxication from opioids or other CNS drugs, especially benzodiazepines
- Adjust dose according to needs

Principles of Medical Management

Evaluate and Treat Medical Conditions

- Reduce risk of contracting or transmitting infectious disease (HIV, hepatitis, TB)
- Consider non-narcotic treatment options for pain management first
- Evaluate cross tolerance with narcotics
- Avoid narcotics that produce withdrawal such as buprenorphine, butorphanol, dezocine, nalbuphine, and pentazocine [Talwin, “T’s,” and tripelennamine, PBZ, “Blues”]

Induction Phase

- Suppress withdrawal symptoms
- Extinguish cravings for opioids
- Block the reinforcing effects of illicit opioid use
- Initial dose 20 to 30 mg usually safe and effective, may use 40 mg if able to show withdrawal after first dose
- Adequacy of dose based on response at three to eight hours after dose, not after 24 hours
- Patient may need *more time*, not more methadone

Induction Phase

Risk of death during methadone induction has been calculated as nearly 7 fold greater than prior to entering treatment and nearly 98 percent greater for new patients than for patients who have been receiving methadone safely for more than two weeks

Induction Phase

- Death usually occurs during the first three to ten days of treatment, at home during sleep, many hours after peak levels have occurred
- Doses that would be safe and effective ordinarily can lead to fatal overdose
- Related to abnormal methadone metabolism or other metabolic or pharmacologic factors
- Depends on initial tolerance, i.e., dose in excess of established tolerance can lead to overdose

Induction Phase

- Methadone levels may rise up to 7 fold during induction with no change in dose
- Ordinarily methadone levels continue to rise for roughly five days after increasing the dose
- Methadone stored extensively in the liver and secondarily in other body tissues
- Toxic accumulation can occur two weeks after initial dose

Stabilization

- Steady-state achieved after four to five half-lives, for methadone usually four to five days
- Once at steady state, methadone should be present in sufficient levels to maintain therapeutic “comfort range”
- On average 80 to 120 mg of methadone sufficient for many patients

Stabilization

- Higher doses are often necessary and safe, provided that dose increases are modest and there is sufficient time between dose changes
- Criteria for higher doses include continued signs or symptoms of withdrawal (may be subjective), persistent cravings for opioids, continued use of illicit opioid drugs

Stabilization

- No clear relationship between dose of methadone and prior tolerance to opioids
- Serum methadone levels usually around 400 ng/mL, but does not always correlate to effective dose of methadone
- Rapid metabolism of methadone in small number of patients and medications that affect cytochrome P450
- Patients may provide false information at any time in a misguided effort to obtain more methadone (results can be fatal)

Maintenance Phase

- Patients receiving higher methadone doses compared with those receiving lower doses demonstrate better outcomes, as measured by absence of illicit drug use and retention in treatment
- Patients at high doses have reduced risk of fatal heroin overdose
- Correct dose of methadone is “enough”

Maintenance Phase

- Correct dose of methadone enables patients to achieve greater stability in their lives, a greater sense of “normalcy”
- Improved attendance at work
- Greater stability with spouse, children, family, and friends
- Improvements in mood, sleep, health
- Criminal activity reduced or eliminated
- Financial situation becomes manageable

Goals of Maintenance Therapy

- Prevent or reduce withdrawal symptoms
- Prevent or reduce drug craving(s)
- Prevent relapse to addictive drug(s)

Maintenance Dose

- Dose range 60 to 120 mg of methadone daily for most maintenance patients
- Some require less, some require more
- Factors that influence the maintenance dose include individual rate of metabolism, medical disease such as hepatitis or HIV, medications, illicit drugs, other substances and grapefruit juice

Urine Toxicology

- Opiates
- Propoxyphene
- Benzodiazepines
- Barbiturates
- Cocaine (benzoylecognine)
- Amphetamine
- Cannabinoids

Detoxification

- Gradual reduction of dose over several days to weeks
- Small changes in dose less likely to produce withdrawal syndrome
- Many patients experience difficult when dose drops below 40 mg
- At risk for using opiates or other drugs, especially benzodiazepines or alcohol

Pregnancy

- Safest recommendation is for pregnant woman to be taking no medications or using illicit drugs
- Consider taper from methadone if female patient wishes to achieve pregnancy
- Most situations, patient on maintenance dose and becomes pregnant
- Safest recommendation is to stay on methadone for the entire pregnancy

Pain Management

- Do not interrupt daily dose of methadone
- Dose may be divided for surgery: 50% of usual dose before surgery and 50% after surgery
- Reassure patient will receive adequate doses of pain medication
- Short-acting opioid agonists should be used in higher and more frequent doses

Pain Management

- Do not use partial agonists such as buprenorphine, butorphanol, dezocine, nalbuphine, or pentazocine
- Change to nonnarcotic agents as soon as practical
- Avoid prescribing for self-administration
- Request for increase in dose of methadone not effective

Sources

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